L Number	Hits	Search Text	DB	Time stamp
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NEWS 4	Apr 09	ZDB will be removed from STN
NEWS 5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
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NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
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NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS 15	Jul 30	NETFIRST to be removed from STN
NEWS 16	Aug 08	CANCERLIT reload
NEWS 17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18	Aug 08	NTIS has been reloaded and enhanced
NEWS 19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
NEWS 24	Sep 16	Experimental properties added to the REGISTRY file
NEWS 25	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 26	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 27	Oct 21	EVENTLINE has been reloaded
NEWS 28	Oct 24	BEILSTEIN adds new search fields
NEWS 29	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 30	Oct 25	MEDLINE SDI run of October 8, 2002
NEWS 31	Nov 18	DKILIT has been renamed APOLLIT
NEWS 32	Nov 25	More calculated properties added to REGISTRY
NEWS 33	Dec 02	TIBKAT will be removed from STN
NEWS 34	Dec 04	CSA files on STN
NEWS 35	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 36	Dec 17	TOXCENTER enhanced with additional content
NEWS 37	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 38	Dec 30	ISMEC no longer available
NEWS 39	Jan 13	Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 40	Jan 21	NUTRACEUT offering one free connect hour in February 2003
NEWS 41	Jan 21	PHARMAML offering one free connect hour in February 2003
NEWS 42	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 43	Feb 13	CANCERLIT is no longer being updated
NEWS 44	Feb 24	METADEX enhancements
NEWS 45	Feb 24	PCTGEN now available on STN

NEWS 46 Feb 24 TEMA now available on STN
NEWS 47 Feb 26 NTIS now allows simultaneous left and right truncation
NEWS 48 Feb 26 PCTFULL now contains images
NEWS 49 Mar 04 SDI PACKAGE for monthly delivery of multifile SDI results

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  77 FILES SEARCHED...
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=> s (mutation or mutant or mutated) (2a) lactamase
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L2   1713 (MUTATION OR MUTANT OR MUTATED) (2A) LACTAMASE

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AN 2002:147183 BIOSIS
DN PREV200200147183
TI Insertion of dibasic residues directs a constitutive protein to the regulated secretory pathway.
AU Feliciangeli, Sylvain; Kitabgi, Patrick (1)
CS (1) Institut de Pharmacologie Moleculaire et Cellulaire, CNRS-UMR 6097, 660 Route des Lucioles, 06560, Valbonne: kitabgi@ipmc.cnrs.fr France
SO Biochemical and Biophysical Research Communications, (January 11, 2002) Vol. 290, No. 1, pp. 191-196. http://www.academicpress.com/bbrc. print. ISSN: 0006-291X.
DT Article
LA English
AB The mechanisms for sorting proteins to the regulated secretory pathway (RSP) remains poorly understood. We recently reported that dibasic sequences that are cleaved by pro-protein convertases (PCs) in pro-neurotensin also acted as sorting signal for the precursor. Here we addressed two questions regarding the role of dibasics as sorting signal: (i) Are dibasics sufficient to direct proteins to the RSP? (ii) Do they sort proteins by virtue of their interaction with PCs? The first question was studied by inserting dibasics in beta-lactamase, a constitutively secreted protein and comparing the regulated secretion of beta-lactamase to that of its mutant in transfected endocrine cells. The second question was investigated by comparing the regulated release of pro-neurotensin in PC12 cells that are devoid of PCs to that in PC1- and PC2-transfected PC12 cells. The data show that the **mutant** beta-**lactamase** was indeed **targeted** in part to the RSP and that pro-neurotensin was sorted to the RSP without the assistance of the PCs, thus indicating that dibasics can act as sorting signal by themselves independently of their interaction with PCs.

L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 2
AN 2001:489911 CAPLUS
DN 135:75844
TI Composition, method and system for identifying novel antimicrobial agents
IN Palzkill, Timothy G.; Petrosino, Joseph; Huang, Wanzhi
PA USA
SO U.S. Pat. Appl. Publ., 17 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2001006959	A1	20010705	US 1998-160405	19980925
	US 2001007754	A1	20010712	US 1999-318476	19990525
PRAI	US 1998-160405	A2	19980925		

AB A compn., method and system for identifying novel antimicrobial agents including the steps of, displaying a .beta.-lactamase inhibitor protein on a virus, contacting the virus with a .beta.-**lactamase** binding protein **target**, selecting for the virus that has a higher affinity for the target and testing the .beta.-lactamase inhibitor protein for antimicrobial activity, is disclosed. The invention also includes a nucleic acid encoding a fusion protein comprising a .beta.-lactamase inhibitor protein and an affinity carrier and the protein expressed therefrom. **Mutant** .beta.-**lactamase** inhibitor proteins

may be produced, characterized, isolated and expressed in prokaryotic cells and used as antimicrobial agents.

L4 ANSWER 3 OF 7 USPATFULL
AN 2001:109872 USPATFULL
TI SMALL MOLECULE DRUG SCREEN
IN PALZKILL, TIMOTHY G., HOUSTON, TX, United States
PETROSINO, JOSEPH, HOUSTON, TX, United States
HUANG, WANZHI, HOUSTON, TX, United States
PI US 2001007754 A1 20010712
AI US 1999-318476 A1 19990525 (9)
RLI Continuation-in-part of Ser. No. US 1998-160405, filed on 25 Sep 1998, PENDING
DT Utility
FS APPLICATION
LREP DANIEL F PEREZ, GARDERE & WYNNE LLP, 3000 THANKSGIVING TOWER, 1601 ELM STREET, DALLAS, TX, 75201
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 1216
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A system for identifying novel antimicrobial agents is disclosed that includes the steps of attaching a .beta.-**lactamase** inhibitor protein **target** to a solid support, exposing the .beta.-**lactamase** inhibitor protein **target** to a .beta.-lactamase inhibitor protein and an analyte, and detecting the effect of the analyte on the binding of the .beta.-lactamase protein to its protein target, wherein a decrease in binding between the .beta.-**lactamase** protein **target** and the .beta.-lactamase inhibitor protein indicates that the analyte affects the interaction between .beta.-lactamase inhibitor protein and its protein target.

L4 ANSWER 4 OF 7 USPATFULL
AN 2001:173572 USPATFULL
TI Antibacterial and antibiotic methods using peptide nucleic acids and pharmaceutical compositions therefor
IN Nielsen, Peter E., Hjortevanget 509, DK 2980, Kokkedal, Denmark
Good, Liam, Copenhagen, Denmark
PA Nielsen, Peter E., Denmark (non-U.S. individual)
PI US 6300318 B1 20011009
AI US 1997-932140 19970916 (8)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Marschel, Ardin H.
LREP Woodcock Washburn Kurtz Mackiewicz & Norris LLP
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1332
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods of and compositions for killing or inhibiting the growth of a bacteria are disclosed. The methods comprise the use of peptide nucleic acid that is targeted to mRNA and/or rRNA. In certain embodiments, methods include the use of one or more separate antibiotics.

L4 ANSWER 5 OF 7 USPATFULL
AN 2001:25631 USPATFULL
TI Methods of bacterial gene function determination using peptide nucleic acids
IN Nielsen, Peter E., Hjortevanget 509, DK 2980, Kokkedal, Denmark
Good, Liam, Copenhagen, Denmark
PA Nielsen, Peter E., Kokkedel, Denmark (non-U.S. individual)
PI US 6190866 B1 20010220

AI US 1998-49190 19980327 (9)
RLI Continuation-in-part of Ser. No. US 1997-932140, filed on 16 Sep 1997
DT Utility
FS Granted
EXNAM Primary Examiner: Marschel, Ardin H.
LREP Woodcock Washburn Kurtz Mackiewicz & Norris LLP
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1462
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods of and compositions for killing or inhibiting the growth of a bacteria are disclosed. Methods of determing bacterial gene functions are also disclosed. The methods comprise the use of peptide nucleic acid that is targeted to mRNA and/or rRNA. In certain embodiments, methods include the use of one or more separate antibiotics.

L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS
AN 2000:456065 CAPLUS
DN 133:131477
TI Mechanism-based selection and labeling of biocatalysts
AU Lo, Lee-Chiang
CS Department of Chemistry, National Taiwan University, Taipei, 106, Taiwan
SO Huaxue (2000), 58(1), 201-204
CODEN: HUHSA2; ISSN: 0441-3768
PB Chinese Chemical Society
DT Journal; General Review
LA Chinese
AB A review with 3 refs. Labeling and selection of biocatalysts by their reaction mechanism is a new approach that can provide a fast and efficient way to identify and locate designated hydrolytic activities. The key part of this approach is the design and synthesis of activity probes. In this article, we present two examples of activity probe design **targeting mutant** .beta.-**lactamase** and catalytic antibodies of .beta.-galactosidase activity by screening their phage-displayed libraries.

L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS
AN 1998:745098 CAPLUS
DN 130:13213
TI Recombinant single-chain antibody-.beta.-**lactamase** fusion protein **targets** melanoma cells
IN Siemers, Nathan O.; Yarnold, Susan; Senter, Peter D.
PA Bristol-Myers Squibb Co., USA
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9850432	A1	19981112	WO 1998-US8840	19980430
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9872748	A1	19981127	AU 1998-72748	19980430
	EP 986576	A1	20000322	EP 1998-920103	19980430
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

	US 6132722	A	20001017	US 1998-70637	19980430
	JP 2002510968	T2	20020409	JP 1998-548240	19980430
PRAI	US 1997-45888P	P	19970507		
	US 1998-70637	A	19980430		
	WO 1998-US8840	W	19980430		

AB The authors disclose a recombinant fusion polypeptide comprising antibody VH and VL sequences operatively linked in a single-chain scFv format to .beta.-lactamase. The scFv-.beta.-lactamase fusion protein recognized the tumor-assocd. antigen melanotransferrin and exhibited biol. activity against melanoma cells in conjunction with the cephalosporin mustard prodrug CCM.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
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NEWS 7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
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NEWS 11	Jun 10	PCTFULL has been reloaded
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NEWS 18	Aug 08	NTIS has been reloaded and enhanced
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NEWS 20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
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NEWS 25	Sep 16	CA Section Thesaurus available in CAPLUS and CA
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NEWS 30	Oct 25	MEDLINE SDI run of October 8, 2002
NEWS 31	Nov 18	DKILIT has been renamed APOLLIT
NEWS 32	Nov 25	More calculated properties added to REGISTRY
NEWS 33	Dec 02	TIBKAT will be removed from STN
NEWS 34	Dec 04	CSA files on STN
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NEWS 36	Dec 17	TOXCENTER enhanced with additional content
NEWS 37	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 38	Dec 30	ISMEC no longer available
NEWS 39	Jan 13	Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 40	Jan 21	NUTRACEUT offering one free connect hour in February 2003
NEWS 41	Jan 21	PHARMAML offering one free connect hour in February 2003
NEWS 42	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 43	Feb 13	CANCERLIT is no longer being updated
NEWS 44	Feb 24	METADEX enhancements
NEWS 45	Feb 24	PCTGEN now available on STN
NEWS 46	Feb 24	TEMA now available on STN
NEWS 47	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 48	Feb 26	PCTFULL now contains images

NEWS 49 Mar 04 SDI PACKAGE for monthly delivery of multifile SDI results

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L3         2831 (MUTANT OR MUTATE OR MUTATION OR MUTATED) (4A) LACTAMASE

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  29 FILES SEARCHED...
  56 FILES SEARCHED...
  90 FILES SEARCHED...
L4           10 L2 AND L3
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=> d l4 1-10 bib ab

L4 ANSWER 1 OF 10 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1997:486725 BIOSIS
DN PREV199799785928
TI Dissemination of antibiotic resistance.
AU Roy, Paul H.
CS Cent. Rech. Cent. Hosp. Univ. Laval, Dep. Biochim., Univ. Laval, 2705 boulevard Laurier, Sainte-Foy, PQ G1V 4G2 Canada
SO M-S (Medecine Sciences), (1997) Vol. 13, No. 8-9, pp. 927-933. ISSN: 0767-0974.
DT General Review
LA French
SL French; English
AB While antibiotics have, for the past fifty years, been "miracle drugs", we are presently facing the "end of the miracle". The increasing use of antibiotics has led to the selection of bacteria resistant to multiple antibiotics. Diverse mechanisms of resistance are found in resistant bacteria. Among these are enzymatic degradation or alteration of antibiotic molecules (e.g. beta-lactamases and aminoglycoside modifying enzymes), altered targets (e.g. penicillin-binding proteins and dihydrofolate reductase), and drug efflux (e.g. of tetracycline). Often point mutations can drastically alter the enzyme or the **target**: beta-**lactamases** become able to digest third-generation cephalosporins, dihydrofolate reductase becomes resistant to trimethoprim, and DNA gyrase becomes resistant to quinolones. Resistance genes have not always been present in common pathogenic bacteria, but have been evolving in antibiotic producing bacteria or in those cohabiting with them in the environment, and have recently been acquired by horizontal transfer. Many resistance genes are on conjugative plasmids of wide host range, often as part of transposons. Examples are the TEM beta-**lactamase**, whose gene can **mutate** to yield resistance to third-generation cephalosporins, and vancomycin resistance in enterococci, where a complete metabolic pathway for an altered cell wall in encoded by a transposon. In addition, a novel DNA element called an integron has been described, in which individual resistance genes exist as mobile cassettes and are rearranged by site-specific recombination, in a sort of natural genetic engineering, to form strongly expressed multiresistance operons. Knowledge of the mechanisms of resistance gene evolution and dissemination and of antibiotic usage patterns leads to the prediction, in a more or less immediate future, of the emergence of vancomycin-resistant staphylococci, of multiresistant pneumococci, and of third-generation-cephalosporin-resistant Haemophilus and Neisseria, for which the medical community must be prepared.

L4 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2003 ACS
AN 2001:489911 CAPLUS
DN 135:75844
TI Composition, method and system for identifying novel antimicrobial agents
IN Palzkill, Timothy G.; Petrosino, Joseph; Huang, Wanzhi
PA USA
SO U.S. Pat. Appl. Publ., 17 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2001006959	A1	20010705	US 1998-160405	19980925
	US 2001007754	A1	20010712	US 1999-318476	19990525
PRAI	US 1998-160405	A2	19980925		

AB A compn., method and system for identifying novel antimicrobial agents

including the steps of, displaying a .beta.-lactamase inhibitor protein on a virus, contacting the virus with a .beta.-**lactamase** binding protein **target**, selecting for the virus that has a higher affinity for the target and testing the .beta.-lactamase inhibitor protein for antimicrobial activity, is disclosed. The invention also includes a nucleic acid encoding a fusion protein comprising a .beta.-lactamase inhibitor protein and an affinity carrier and the protein expressed therefrom. **Mutant** .beta.-**lactamase** inhibitor proteins may be produced, characterized, isolated and expressed in prokaryotic cells and used as antimicrobial agents.

L4 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2003 ACS
AN 2000:456065 CAPLUS
DN 133:131477
TI Mechanism-based selection and labeling of biocatalysts
AU Lo, Lee-Chiang
CS Department of Chemistry, National Taiwan University, Taipei, 106, Taiwan
SO Huaxue (2000), 58(1), 201-204
CODEN: HUHSA2; ISSN: 0441-3768
PB Chinese Chemical Society
DT Journal; General Review
LA Chinese
AB A review with 3 refs. Labeling and selection of biocatalysts by their reaction mechanism is a new approach that can provide a fast and efficient way to identify and locate designated hydrolytic activities. The key part of this approach is the design and synthesis of activity probes. In this article, we present two examples of activity probe design **targeting mutant** .beta.-**lactamase** and catalytic antibodies of .beta.-galactosidase activity by screening their phage-displayed libraries.

L4 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2003 ACS
AN 1998:745098 CAPLUS
DN 130:13213
TI Recombinant single-chain antibody-.beta.-**lactamase** fusion protein **targets** melanoma cells
IN Siemers, Nathan O.; Yarnold, Susan; Senter, Peter D.
PA Bristol-Myers Squibb Co., USA
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9850432	A1	19981112	WO 1998-US8840	19980430
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9872748	A1	19981127	AU 1998-72748	19980430
	EP 986576	A1	20000322	EP 1998-920103	19980430
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6132722	A	20001017	US 1998-70637	19980430
	JP 2002510968	T2	20020409	JP 1998-548240	19980430
PRAI	US 1997-45888P	P	19970507		
	US 1998-70637	A	19980430		
	WO 1998-US8840	W	19980430		

AB The authors disclose a recombinant fusion polypeptide comprising antibody

VH and VL sequences operatively linked in a single-chain scFv format to .beta.-lactamase. The scFv-.beta.-lactamase fusion protein recognized the tumor-assocd. antigen melanotransferrin and exhibited biol. activity against melanoma cells in conjunction with the cephalosporin mustard prodrug CCM.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 10 USPATFULL
AN 2002:301193 USPATFULL
TI Binding and catalysis screen for high throughput determination of protein function using chemical inducers of dimerization
IN Cornish, Virginia W., New York, NY, UNITED STATES
PI US 2002168737 A1 20021114
AI US 2001-768474 A1 20010124 (9)
DT Utility
FS APPLICATION
LREP John P. White, Cooper & Dunham LLP, 1185 Avenue of the Americas, New York, NY, 10036
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN 25 Drawing Page(s)
LN.CNT 1784
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for screening a cDNA library by identifying the expressed protein target, comprising:

(a) providing a screening molecule comprising a methotrexate moiety or an analog of methotrexate covalently bonded to a ligand which has a known specificity;

(b) introducing the screening molecule into a cell which expresses a first fusion protein comprising a binding domain capable of binding methotrexate, a second fusion protein comprising the expressed unknown protein target, and a reporter gene wherein expression of the reporter gene is conditioned on the proximity of the first fusion protein to the second fusion protein;

(c) permitting the screening molecule to bind to the first fusion protein and to the second fusion protein so as to activate the expression of the reporter gene;

(d) selecting which cell expresses the reporter gene; and

(e) identifying the unknown protein target and the corresponding cDNA.

L4 ANSWER 6 OF 10 USPATFULL
AN 2002:301142 USPATFULL
TI Covalent chemical inducers of protein dimerization and their uses in high throughput binding screens
IN Cornish, Virginia W., New York, NY, UNITED STATES
PI US 2002168685 A1 20021114
AI US 2002-56874 A1 20020124 (10)
RLI Continuation-in-part of Ser. No. US 2001-768474, filed on 24 Jan 2001, PENDING
DT Utility
FS APPLICATION
LREP John P. White, Cooper & Dunham LLP, 1185 Avenue of the Americas, New York, NY, 10036
CLMN Number of Claims: 54
ECL Exemplary Claim: 1
DRWN 24 Drawing Page(s)
LN.CNT 1954
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Described are compounds having the formula:

H1-Y-H2

where H1 is a substrate capable of selectively binding to a first receptor; where H2 is a substrate capable of selectively binding to and selectively forming a covalent bond with a second receptor; and wherein Y is a moiety providing a covalent linkage between H1 and H2, which may be present or absent, and when absent, H1 is covalently linked to H2. Also described are uses of the compounds for in vivo screening of compounds and proteins.

L4 ANSWER 7 OF 10 USPATFULL
AN 2002:214254 USPATFULL
TI Beta-lactam antibiotics
IN Chan, Ming Fai, Encinitas, CA, UNITED STATES
Castillo, Rosario S., San Diego, CA, UNITED STATES
Li, Qing, La Jolla, CA, UNITED STATES
Doppalapudi, Venkata Ramana, San Diego, CA, UNITED STATES
Hixon, Mark Stephen, San Diego, CA, UNITED STATES
Lobl, Thomas J., Foster City, CA, UNITED STATES
PI US 2002115642 A1 20020822
AI US 2001-847525 A1 20010501 (9)
PRAI US 2000-201642P 20000502 (60)
DT Utility
FS APPLICATION
LREP BAKER & MCKENZIE, 660 HANSEN WAY, PALO ALTO, CA, 94304
CLMN Number of Claims: 73
ECL Exemplary Claim: 1
DRWN 14 Drawing Page(s)
LN.CNT 2528
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides compositions comprising improved beta-lactam antibiotics and methods for applying these compositions to inhibit the growth of microbial infections. The improved antibiotics are capable of inhibiting the growth of both antibiotic sensitive and antibiotic resistant microorganisms In addition, the invention provides methods for treating a subject infected with a microorganism by administering the compositions of the invention.

L4 ANSWER 8 OF 10 USPATFULL
AN 2001:173572 USPATFULL
TI Antibacterial and antibiotic methods using peptide nucleic acids and pharmaceutical compositions therefor
IN Nielsen, Peter E., Hjortevanget 509, DK 2980, Kokkedal, Denmark
Good, Liam, Copenhagen, Denmark
PA Nielsen, Peter E., Denmark (non-U.S. individual)
PI US 6300318 B1 20011009
AI US 1997-932140 19970916 (8)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Marschel, Ardin H.
LREP Woodcock Washburn Kurtz Mackiewicz & Norris LLP
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1332
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods of and compositions for killing or inhibiting the growth of a bacteria are disclosed. The methods comprise the use of peptide nucleic acid that is targeted to mRNA and/or rRNA. In certain embodiments, methods include the use of one or more separate antibiotics.

L4 ANSWER 9 OF 10 USPATFULL

AN 2000:167754 USPATFULL
TI Application of enzyme prodrugs as anti-infective agents
IN Shepard, H. Michael, Rancho Santa Fe, CA, United States
PA NewBiotics, Inc., San Diego, CA, United States (U.S. corporation)
PI US 6159706 20001212
AI US 1998-215688 19981218 (9)
PRAI US 1997-68703P 19971223 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Minnifield, Nita; Assistant Examiner: Baskar, Padma
LREP Konski, Antoinette F.Baker & McKenzie
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 829
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a method for targeting toxic antimetabolites to gram negative infections. It provides a means of taking advantage of a key disease resistance mechanism to activate these drugs locally, and to overcome the resistance phenotype of the microbes. The invention further provides a method for selecting for antibiotic sensitivity, since a likely mechanism by which organisms are likely to gain resistance to the prodrugs is via loss of enzyme activity, which will make the bacteria sensitive to antibiotics once again.

L4 ANSWER 10 OF 10 WPINDEX (C) 2003 THOMSON DERWENT
AN 2001-589860 [66] WPINDEX
DNC C2001-174878
TI New beta-lactam prodrugs, useful for selectively inhibiting the proliferation of antibiotic resistant microorganisms.
DC B02
IN CATHERS, B E; CHAN, M F; DOPPALAPUDI, V R; HIXON, M S; LOBL, T J; SHEPARD, H M
PA (NEWB-N) NEWBIOTICS INC
CYC 95
PI WO 2001064687 A1 20010907 (200166)* EN 46p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001041878 A 20010912 (200204)
EP 1263762 A1 20021211 (200301) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2001064687 A1 WO 2001-US6519 20010227; AU 2001041878 A AU 2001-41878 20010227; EP 1263762 A1 EP 2001-913190 20010227, WO 2001-US6519 20010227
FDT AU 2001041878 A Based on WO 200164687; EP 1263762 A1 Based on WO 200164687
PRAI US 2000-185479P 20000228
AB WO 200164687 A UPAB: 20011113
NOVELTY - Beta-Lactam prodrugs (I) are new, and selectively inhibit the proliferation of antibiotic resistant microorganisms by targeting toxic anti-metabolites to antibiotic resistant microbial infections.
DETAILED DESCRIPTION - A prodrug compound of formula (I) is new:
R' = H, alkyl, aryl, halogenated aryl, nitro aryl, phenol, ammonium, methylamine, dimethylamine, lower alkylamine, bis(lower alkyl)amine, glycol, glycerol, sorbitol, polyethylene glycol, salt form (sodium, potassium, lithium), 2-amino-2-hydroxymethyl-1,3-propanediol;
X = absent or carbonyl, methylene, O, S or N;
Y = methylene, methyl alkenyl, methylene alkynyl, methyleneoxycarbonyl, vinyl or 1-6C alkynyl; or
X+Y = =CH-CH2, H2C-CH=, or a group of formula (i):
T = O, N, S or C;

Z = a toxophore or is absent.

An INDEPENDENT CLAIM is included for the following:

(a) an in vitro method for assaying drugs that inhibit or kill antibiotic resistant microorganisms, comprising contacting the drug with an antibiotic resistant microorganism, and separately contacting the microorganism with a compound (I); then comparing the growth of the microorganisms;

(b) a method for inhibiting the growth of or killing a microorganism comprising contacting the microorganism first with an antibiotic and subsequently with a compound of formula (I); and

(c) a method for reversing antibiotic resistance in a microorganism by contacting the microorganism with (I).

ACTIVITY - Antibacterial.

Test details are described but no results given.

MECHANISM OF ACTION - Bactericidal agent formation; penicillin protein binding inhibitors.

(I) can kill bacteria by formation of bactericide in beta -lactamase producing strains. They also have cidal activity against non- beta lactamase strains by inhibiting cell wall biosynthesis.

USE - For reversing antibiotic resistance in a microorganism, and for treating antibiotic resistant infections, e.g. where the antibiotic resistant microorganism is a beta -lactam resistant (gram-positive or gram-negative) or vancomycinresistant microorganism. The gram-positive bacteria include Staphylococcus aureus, Staph.epidermis, coagulase-negative staphylococci, Streptococcus pyogenes, Strep.pneumoniae, Strep.agalactiae and Enterococcus. Gram-negative bacteria include Neisseria, Moraxella, Campylobacter, Enterobacteriaceae, Pseudomonas, Actinetobacter, Haemophilus and Bacteroides.

(I) can be used in plants or vertebrates (a fish, mammal or avian).

ADVANTAGE - The prodrugs can be activated by any beta lactamase, avoiding the problem of selecting the proper beta lactamase inhibitor. A single prodrug will be activated by beta lactamases of many species of bacteria, and can be used to treat infections previously resistant to treatment because of high levels of beta -**lactamase** production by the **target** organism. This approach avoids the problem of **mutation** resistance encountered with beta -**lactamase** inhibitors. Resistance to the prodrugs is likely to come about via the loss of beta -lactamase activity, which will result in the bacterium regaining sensitivity to the penicillins.

Dwg.0/0

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<------User Break------>

L2 ANSWER 89 OF 109 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
DUPLICATE 32
AN 1984:312889 BIOSIS
DN BA78:49369
TI THE EFFECT OF BETA **LACTAMASE** STABILITY PENETRATION AND **TARGET** AFFINITY ON THE ACTIVITY OF CEFAZOLIN CEFAMANDOLE CEFOXITIN AND CEFUROXIME.
AU HARPER P B
CS MICROBIOL. DIV., GLAXO GROUP RESEARCH, GREENFORD, MIDDLESEX, ENGLAND.
SO CLIN THER, (1984) 6 (3), 310-324.
CODEN: CLTHDG. ISSN: 0149-2918.
FS BA; OLD
LA English

L2 ANSWER 37 OF 109 USPATFULL
AN 2000:167754 USPATFULL
TI Application of enzyme prodrugs as anti-infective agents
IN Shepard, H. Michael, Rancho Santa Fe, CA, United States
PA NewBiotics, Inc., San Diego, CA, United States (U.S. corporation)
PI US 6159706 20001212
AI US 1998-215688 19981218 (9)
PRAI US 1997-68703P 19971223 (60)
DT Utility
FS Granted
LN.CNT 829
INCL INCLM: 435/032.000
INCLS: 435/030.000; 435/043.000; 435/006.000; 435/002.000; 424/009.100; 530/300.000; 530/335.000; 514/016.000; 514/018.000; 514/199.000; 514/206.000; 514/204.000; 514/203.000; 514/246.000; 540/222.000; 540/225.000
NCL NCLM: 435/032.000
NCLS: 424/009.100; 435/002.000; 435/006.000; 435/030.000; 435/043.000; 514/016.000; 514/018.000; 514/199.000; 514/203.000; 514/204.000; 514/206.000; 514/246.000; 530/300.000; 530/335.000; 540/222.000; 540/225.000
IC [7]
ICM: C12Q001-18
ICS: C12Q001-26; C07D005-00; A61K038-00; A61K031-43
EXF 435/2; 435/6; 435/43; 435/32; 435/30; 424/9.1; 424/16.18; 514/199; 514/206; 514/204; 514/203; 514/246; 530/335; 530/300; 540/222; 540/225; 540/227; 544/21; 542/418
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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NEWS 3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4	Apr 09	ZDB will be removed from STN
NEWS 5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
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NEWS 18	Aug 08	NTIS has been reloaded and enhanced
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NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
NEWS 24	Sep 16	Experimental properties added to the REGISTRY file
NEWS 25	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 26	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 27	Oct 21	EVENTLINE has been reloaded
NEWS 28	Oct 24	BEILSTEIN adds new search fields
NEWS 29	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 30	Oct 25	MEDLINE SDI run of October 8, 2002
NEWS 31	Nov 18	DKILIT has been renamed APOLLIT
NEWS 32	Nov 25	More calculated properties added to REGISTRY
NEWS 33	Dec 02	TIBKAT will be removed from STN
NEWS 34	Dec 04	CSA files on STN
NEWS 35	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 36	Dec 17	TOXCENTER enhanced with additional content
NEWS 37	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 38	Dec 30	ISMEC no longer available
NEWS 39	Jan 13	Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 40	Jan 21	NUTRACEUT offering one free connect hour in February 2003
NEWS 41	Jan 21	PHARMAML offering one free connect hour in February 2003
NEWS 42	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 43	Feb 13	CANCERLIT is no longer being updated
NEWS 44	Feb 24	METADEX enhancements
NEWS 45	Feb 24	PCTGEN now available on STN
NEWS 46	Feb 24	TEMA now available on STN
NEWS 47	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 48	Feb 26	PCTFULL now contains images
NEWS 49	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results

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  75 FILES SEARCHED...
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 100 FILES SEARCHED...
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               ON) (4A) (SITE OR MOTIF OR DOMAIN)

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  29 FILES SEARCHED...
  40 FILES SEARCHED...
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L6 ANSWER 385 OF 926 USPATFULL
AN 2001:33062 USPATFULL
TI .alpha.-Amylase variants
IN Svendsen, Allan, Birkerod, Denmark
Kjaerulff, Soeren, Vanlose, Denmark
Bisgaard-Frantzen, Henrik, Bagsvaerd, Denmark
Andersen, Carsten, Vaerloese, Denmark
PA Novo-Nordisk A/S, Bagsvaerd, Denmark (non-U.S. corporation)
Novo Alle, Bagsvaerd, Denmark (non-U.S. corporation)
PI US 6197565 B1 20010306
AI US 1998-193068 19981116 (9)
DT Utility
FS Granted
EXNAM Primary Examiner: Prouty, Rebecca E.; Assistant Examiner: Hutson, Richard
LREP Lambiris, Esq., Elias J.
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 1279
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to a variant of a parent Termamyl-like .alpha.-amylase, comprising mutations in two, three, four, five or six regions/positions. The variants have increased stability at high temperatures (relative to the parent). The invention also relates to a DNA construct comprising a DNA sequence encoding an .alpha.-amylase variant of the invention, a recombinant expression vector which carries a DNA construct of the invention, a cell which is transformed with a DNA construct of the invention, the use of an .alpha.-amylase variant of the invention for washing and/or dishwashing, textile desizing, starch liquefaction, a detergent additive comprising an .alpha.-amylase variant of the invention, a manual or automatic dishwashing detergent composition comprising an .alpha.-amylase variant of the invention, a method for generating a variant of a parent Termamyl-like .alpha.-amylase, which variant exhibits increased.

L6 ANSWER 389 OF 926 USPATFULL
AN 2001:25665 USPATFULL
TI Subtilase variants
IN Sierkstra, Laurens Nicolaas, Delft, Netherlands
Klugkist, Jan, Vlaardingen, Netherlands
Markvardsen, Peter, Bagsv.ae butted.rd, Denmark
von der Osten, Claus, Lyngby, Denmark
Bauditz, Peter, Copenhagen, Denmark
PA Novo Nordisk A/S, Bagsvaerd, Denmark (non-U.S. corporation)
PI US 6190900 B1 20010220
AI US 1998-120577 19980722 (9)
RLI Continuation of Ser. No. US 1996-642987, filed on 6 May 1996, now patented, Pat. No. US 5837517, issued on 17 Nov 1998
PRAI DK 1995-519 19950505
EP 1995-201161 19950505
DK 1996-421 19960412
DT Utility

FS Granted
EXNAM Primary Examiner: Achutamurthy, Ponnathapu; Assistant Examiner: Moore, William W.
LREP Zelson, Esq., Steve T., Lambiris, Esq., Elias J.
CLMN Number of Claims: 51
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 2124
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to enzymes produced by mutating the genes for a number of subtilases and expressing the mutated genes in suitable hosts are presented. The enzymes exhibit improved stability and/or improved wash performance in any detergent in comparison to their wild type parent enzymes. The enzymes are well-suited for use in any detergent and for some in especially liquid or solid shaped detergent compositions.

L6 ANSWER 404 OF 926 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V. DUPLICATE
AN 2001:33022537 BIOTECHNO
TI Critical residues for the specificity of cofactors and substrates in human estrogenic 17.beta.-hydroxysteroid dehydrogenase 1: Variants designed from the three-dimensional structure of the enzyme
AU Huang Y.-W.; Pineau I.; Chang H.-J.; Azzi A.; Bellemare V.; Laberge S.; Lin S.-X.
CS S.-X. Lin, M. R. C. G. M. E. O., Molec. Endocrinology Research Ctr., Laval University Medical Center, 2705 Boulevard Laurier, Quebec, Que. G1V 4G2, Canada.
E-mail: sxlin@crchul.ulaval.ca
SO Molecular Endocrinology, (2001), 15/11 (2010-2020), 47 reference(s)
CODEN: MOENEN ISSN: 0888-8809
DT Journal; Article
CY United States
LA English
SL English
AB Human estrogenic 17.beta.-hydroxysteroid dehydrogenase is an NADP(H)-preferring enzyme. It possesses 11- and 4-fold higher specificity toward NADP(H) over NAD(H) for oxidation and reduction, respectively, as demonstrated by kinetic studies. To elucidate the roles of the amino acids involved in cofactor specificity, we generated **variants** by **site**-directed mutagenesis. The results showed that introducing a positively charged residue, lysine, at the Ser12 position increased the enzyme's preference for NADP(H) more than 20-fold. Substitution of the negatively charged residue, aspartic acid, into the Leu36 position switched the enzyme's cofactor preference from NADPH to NAD with a 220-fold change in the ratio of the specificity toward the two cofactors in the case of oxidation. This **variant** dramatically abolished the **enzyme**'s reductase function and stimulated its dehydrogenase activity, as shown by enzyme activity in intact cells. The substrate-binding pocket was also studied with four variants: Ser142Gly, Ser142Cys, His221Ala, and Glu282Ala. The Ser142Gly **variant** abolished most of the **enzyme**'s oxidation and reduction activities. The residual reductase activity in vitro is less than 2% that of the wild-type **enzyme**. However, the Ser142Cys **variant** was fully inactive, both as a partially purified protein and in intact cells. This suggests that the bulky sulfhydryl group of cysteine entirely disrupted the catalytic triad and that the Ser142 side chain is important for maintaining the integrity of this triad. His221 variation weakened the apparent affinity for estrone, as demonstrated by a 30-fold increase in Michaelis-Menten constant, supporting its important role in substrate binding. This residue may play an important role in substrate inhibition via the formation of a dead-end complex. The formerly suggested

importance of Glu282 could not be confirmed.

L6 ANSWER 422 OF 926 USPATFULL
AN 2000:142125 USPATFULL
TI Heregulin variants
IN Ballinger, Marcus D., Burlingame, CA, United States
Jones, Jennifer T., San Leandro, CA, United States
Fairbrother, Wayne J., Burlingame, CA, United States
Sliwkowski, Mark X., San Carlos, CA, United States
Wells, James A., Burlingame, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
PI US 6136558 20001024
AI US 1998-20880 19980209 (9)
PRAI US 1997-37581P 19970210 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Kemmerer, Elizabeth
LREP McCutchen, Doyle, Brown & Enersen, LLP, Haliday, Emily M.
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 3916
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides heregulin variants that are capable of binding an ErbB receptor. Included in the invention are variants of human heregulins, and, in particular, variants of human heregulin-.beta.1 having enhanced affinity for the ErbB-3 and ErbB-4 receptors. These variants include at least one amino acid substitution and can include further modifications. The invention also provides nucleic acid molecules encoding heregulin variants and related vectors, host cells, pharmaceutical compositions, and methods.

L6 ANSWER 429 OF 926 USPATFULL
AN 2000:113911 USPATFULL
TI Protease variants
IN Rasmussen, Grethe, Copenhagen, Denmark
Nielsen, Egon, Copenhagen, Denmark
Halkier, Torben, Frederiksberg, Denmark
PA Novo Nordisk A/S, Bagsvaerd, Denmark (non-U.S. corporation)
PI US 6110884 20000829
AI US 1999-460658 19991213 (9)
RLI Division of Ser. No. US 1997-852790, filed on 7 May 1997 which is a continuation-in-part of Ser. No. US 1995-522283, filed on 13 Sep 1995, now abandoned which is a continuation-in-part of Ser. No. WO 1993-DK9400133, filed on 29 Mar 1993
DT Utility
FS Granted
EXNAM Primary Examiner: Fries, Kery
LREP Zelson, Steve T., Gregg, Valeta
CLMN Number of Claims: 8
ECL Exemplary Claim: 8
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 790
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention is a protease mutant wherein said mutant substitutes the naturally occurring tyrosine amino acids for other amino acids at positions 91, 167, 171, 192, 209, 214, and 263. The protease mutants are used in detergent compositions.

L6 ANSWER 437 OF 926 USPATFULL
AN 2000:94861 USPATFULL

TI Amylase variants
IN Bisg.ang.rd-Frantzen, Henrik, Lyngby, Denmark
Svendsen, Allan, Birkeroed, Denmark
Borchert, Torben Vedel, Copenhagen N, Denmark
PA Novo Nordisk A/S, Bagsvaerd, Denmark (non-U.S. corporation)
PI US 6093562 20000725
AI US 1996-600656 19960213 (8)
RLI Continuation of Ser. No. WO 1996-DK56, filed on 5 Feb 1996
DT Utility
FS Granted
EXNAM Primary Examiner: Prouty, Rebecca E.
LREP Zelson, Esq., Steve T., Green, Esq., Reza
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 2938
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to variants of a parent .alpha.-amylase, which parent .alpha.-amylase (i) has an amino acid sequence selected from the amino acid sequences shown in SEQ ID No. 1, SEQ ID No. 2, SEQ ID No. 3, and SEQ ID No. 7, respectively; or (ii) displays at least 80% homology with one or more of these amino acid sequences; and/or displays immunological cross-reactivity with an antibody raised against an .alpha.-amylase having one of these amino acid sequences; and/or is encoded by a DNA sequence which hybridizes with the same probe as a DNA sequence encoding an .alpha.-amylase having one of these amino acid sequences; in which variant:

(a) at least one amino acid residue of the parent .alpha.-amylase has been deleted; and/or

(b) at least one amino acid residue of the parent .alpha.-amylase has been replaced by a different amino acid residue; and/or

(c) at least one amino acid residue has been inserted relative to the parent .alpha.-amylase; the variant having .alpha.-amylase activity and exhibiting at least one of the following properties relative to the parent .alpha.-amylase: increased thermostability; increased stability towards oxidation; and reduced Ca.sup.2+ dependency;

with the proviso that the amino acid sequence of the variant is not identical to any of the amino acid sequences shown in SEQ ID No. 1, SEQ ID No. 2, SEQ ID No. 3 and SEQ ID No. 7, respectively.

L6 ANSWER 442 OF 926 USPATFULL
AN 2000:88144 USPATFULL
TI Protease variants
IN Rasmussen, Grethe, Copenhagen, Denmark
Nielsen, Egon, Copenhagen, Denmark
Halkier, Torben, Frederiksberg, Denmark
PA Novo Nordisk A/S, Bagsvaerd, Denmark (non-U.S. corporation)
PI US 6087315 20000711
AI US 1997-852790 19970507 (8)
RLI Continuation of Ser. No. US 1995-522283, filed on 13 Sep 1995, now abandoned which is a continuation of Ser. No. WO 1994-DK133, filed on 29 Mar 1994
PRAI DK 1993-390 19930401
DT Utility
FS Granted
EXNAM Primary Examiner: Fries, Kery
LREP Zelson, Esq., Steve T., Gregg, Esq., Valeta
CLMN Number of Claims: 13

ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 886
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to protease variants, stabilized towards the inactivation caused by peroxidase systems, in which protease variants a naturally occurring tyrosine residue has been deleted or substituted with a different amino acid residue at one or more positions. The invention also relates to a method of stabilizing a protease towards the inactivation caused by peroxidase systems, and detergent compositions comprising a protease variant of the invention.

L6 ANSWER 446 OF 926 USPATFULL
AN 2000:74129 USPATFULL
TI C. antarctica lipase variants
IN Svendsen, Allan, Birker.o slashed.d, Denmark
Pathar, Shamkant Anant, Lyngby, Denmark
Egel-Mitani, Michi, Vedb.ae butted.k, Denmark
Borch, Kim, Copenhagen, Denmark
Clausen, Ib Groth, Hiller.o slashed.d, Denmark
Hansen, Mogens Trier, Lynge, Denmark
PA Novo Nordisk A/S, Bagsvaerd, Denmark (non-U.S. corporation)
PI US 6074863 20000613
WO 9401541 19940120
AI US 1994-360758 19941222 (8)
WO 1993-DK225 19930705
19941222 PCT 371 date
19941222 PCT 102(e) date
PRAI DK 1992-888 19920706
DT Utility
FS Granted
EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Lau, Kawai
LREP Zelson, Esq., Steve T., Gregg, Esq., Valeta
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 1378
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A lipase variant of a parent lipase comprising a trypsin-like catalytic triad including an active serine located in a predominantly hydrophobic, elongated binding pocket of the lipase molecule and, located in a critical position of a lipid contact zone of the lipase structure, an amino acid residue different from an aromatic amino acid residue, which amino acid residue interacts with a lipid substrate at or during hydrolysis, in which lipase variant said amino acid residue has been replaced by an aromatic amino acid residue so as to confer to the variant an increased specific activity as compared to that of the parent lipase. The parent lipase may be a C. antarctica lipase A essentially free from other substances from C. antarctica, which comprises the amino acid sequence shown in SEQ ID No. 2, or a variant of said lipase which (1) has lipase activity, (2) reacts with an antibody reactive with at least one epitope of C. antarctica lipase A having th eamino acid sequence SEQ ID No. 2, and/or (3) is encoded by a nucleotide sequence which hybridizes with an oligonucleotide probe prepared on the basis of the full or partial nucleotide sequence shown in SEQ ID No. 1 encoding the C. antarctica lipase A.

L6 ANSWER 454 OF 926 USPATFULL
AN 2000:34382 USPATFULL
TI Enrichment method for variant proteins with altered binding properties
IN Garrard, Lisa J., Burlingame, CA, United States
Henner, Dennis J., Pacifica, CA, United States

Bass, Steven, Redwood City, CA, United States
Greene, Ronald, Durham, NC, United States
Lowman, Henry B., Hercules, CA, United States
Wells, James A., Burlingame, CA, United States
Matthews, David J., San Francisco, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
PI US 6040136 20000321
AI US 1997-923854 19970903 (8)
RLI Division of Ser. No. US 1995-463587, filed on 5 Jun 1995, now patented, Pat. No. US 5821047 which is a division of Ser. No. US 50058
DT Utility
FS Granted
EXNAM Primary Examiner: Carlson, Karen Cochrane
LREP Winter, Daryl B., Schwartz, Timothy R.
CLMN Number of Claims: 45
ECL Exemplary Claim: 1
DRWN 22 Drawing Figure(s); 20 Drawing Page(s)
LN.CNT 3926
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for selecting novel proteins such as growth hormone and antibody fragment variants having altered binding properties for their respective receptor molecules is provided. The method comprises fusing a gene encoding a protein of interest to the carboxy terminal domain of the gene III coat protein of the filamentous phage M13. The gene fusion is mutated to form a library of structurally related fusion proteins that are expressed in low quantity on the surface of a phagemid particle. Biological selection and screening are employed to identify novel ligands useful as drug candidates. Disclosed are preferred phagemid expression vectors and selected human growth hormone variants.

L6 ANSWER 466 OF 926 USPATFULL
AN 2000:12643 USPATFULL
TI C. antarctica lipase and lipase variants
IN Svendsen, Allan, Birker.o slashed.d, Denmark
Patkar, Shamkant Anant, Lyngby, Denmark
Egel-Mitani, Michi, Vedb.ae butted.k, Denmark
Borch, Kim, Copenhagen, Denmark
Clausen, Ib Groth, Hiller.o slashed.d, Denmark
Hansen, Mogens Trier, Lynge, Denmark
PA Novo Nordisk A/S, Bagsvaerd, Denmark (non-U.S. corporation)
PI US 6020180 20000201
AI US 1998-111556 19980708 (9)
RLI Division of Ser. No. US 1994-360758, filed on 22 Dec 1994 which is a continuation of Ser. No. WO 1993-DK225, filed on 5 Jul 1993
PRAI DK 1992-888 19920706
DT Utility
FS Granted
EXNAM Primary Examiner: Achutamurthy, Ponnathapura; Assistant Examiner: Saidha, Tekchand
LREP Zelson, Esq., Steve T., Gregg, Esq., Valeta
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 1288
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A DNA sequence encoding a lipase having the amino acid sequence shown in SEQ ID NO:2. The lipase has a trypsin-like catalytic triad including an active serine located in a predominantly hydrophobic, elongated binding pocket of the lipase molecule and, located in a critical position of a lipid contact zone of the lipase structure, an amino acid residue different from an aromatic amino acid residue, which amino acid residue

interacts with a lipid substrate at or during hydrolysis, in which lipase variant of the amino acid residue has been replaced by an aromatic amino acid residue so as to confer to the variant an increased specific activity as compared to that of the parent lipase.

L6 ANSWER 471 OF 926 USPATFULL
AN 2000:4641 USPATFULL
TI Method for identifying active domains and amino acid residues in polypeptides and hormone variants
IN Wells, James A., Burlingame, CA, United States
Cunningham, Brian C., Piedmont, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
PI US 6013478 20000111
AI US 1998-104036 19980624 (9)
RLI Continuation of Ser. No. US 1997-903398, filed on 30 Jun 1997, now patented, Pat. No. US 5834250 which is a continuation of Ser. No. US 1995-483039, filed on 6 Jun 1995 which is a continuation of Ser. No. US 1994-190723, filed on 2 Feb 1994, now patented, Pat. No. US 5580723 which is a continuation of Ser. No. US 1992-960227, filed on 13 Oct 1992, now abandoned which is a continuation of Ser. No. US 1992-875204, filed on 27 Apr 1992, now abandoned which is a continuation of Ser. No. US 1989-428066, filed on 26 Oct 1989, now abandoned which is a continuation-in-part of Ser. No. US 1988-264611, filed on 28 Oct 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Achutamurthy, Ponnathapura; Assistant Examiner: Ponnaluni, P.
LREP Schwartz, Timothy R.
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN 59 Drawing Figure(s); 52 Drawing Page(s)
LN.CNT 3184
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides methods for the systematic analysis of the structure and function of polypeptides by identifying active domains which influence the activity of the polypeptide with a **target** substance. Such active **domains** are determined by substituting selected amino acid segments of the polypeptide with an analogous polypeptide segment from an analog to the polypeptide. The analog has a different activity with the target substance as compared to the parent polypeptide. The activities of the segment-substituted polypeptides are compared to the same activity for the parent polypeptide for the target. A comparison of such activities provides an indication of the location of the active domain in the parent polypeptide. The invention also provides methods for identifying the active amino acid residues within the active domain of the parent polypeptide. The method comprises substituting a scanning amino acid for one of the amino acid residues within the active domain of the parent polypeptide and assaying the residue-substituted polypeptide so formed with a target substance. The invention further provides polypeptide variants comprising segment-substituted and residue-substituted growth hormones, prolactins and placental lactogens.

L6 ANSWER 479 OF 926 CAPLUS COPYRIGHT 2003 ACS
AN 1999:48790 CAPLUS
DN 130:106943
TI Variants of Humicola family 6 endo-1,4-.beta.-glucanases CelA and CelB and their use in cleaning compositions
IN Lund, Henrik; Nielsen, Jack Bech; Schulein, Martin; Damgaard, Bo; Andersen, Kim Vilbour

PA Novo Nordisk A/S, Den.
SO PCT Int. Appl., 271 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9901544	A1	19990114	WO 1998-DK299	19980702
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9879088	A1	19990125	AU 1998-79088	19980702
	EP 1002061	A1	20000524	EP 1998-929249	19980702
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				

PRAI DK 1997-813 19970704
WO 1998-DK299 19980702

AB Cleaning compns. are provided comprising one or more enzymes having cellulolytic activity wherein .gtoreq.25% of the total wt. of cellulolytic active protein derives from the presence of a Humicola endo-1,4-.beta.-glucanase or Humicola-like cellulase of the glycolsyl hydrolase family 6. Thus, gene encoding two endo-.beta.-1,4-glucanases (cellulases CelA and CelB) were cloned from Humicola insolens. The 3-dimensional structure of the catalytic core domain of the 2 cellulases were solved by x-ray crystallog. methods. Amino acid sequence alignments with other known cellulases and mol. modeling allowed the identification of residues in the binding cleft of the catalytic core domain, its encompassing loop regions, and on the surface of the 3-dimensional structure. Mutagenesis allowed trimming of the binding cleft loops to increase activity. The CelB enzyme was also stabilized against denaturation by anionic tensides by mutation/deletion of surface exposed residues towards more neg. charged residue(s). The achieve improved performance of the enzyme in color clarification, a linker and cellulose-**binding domain** are attached to the catalytic core domain to achieve a hybrid enzyme. Addnl. variants were constructed. Addnl. variants were constructed (e.g. in positions 20, 56, 94, 95, 103, 182, 183 and 318) with altered pH activity, catalytic properties, and improved detergent compatibility.

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

Have product

L6 ANSWER 480 OF 926 USPATFULL
AN 1999:166831 USPATFULL
TI Cyclomaltodextrin glucanotransferase variants
IN Dijkhuizen, Lubbert, Groningen, Netherlands
Dijkstra, Bauke W., Groningen, Netherlands
Andersen, Carsten, Bagsvaerd, Denmark
Osten, Claus von der, Bagsvaerd, Denmark
PA Novo Nordisk A/S, Bagsv.ae butted.rd, Denmark (non-U.S. corporation)
PI US 6004790 19991221
AI US 1997-947965 19971009 (8)
RLI Continuation of Ser. No. WO 1996-DK179, filed on 22 Apr 1996
PRAI DK 1995-477 19950421
DK 1995-1173 19951017
DK 1995-1281 19951116
DT Utility
FS Granted

EXNAM Primary Examiner: Sisson, Bradley; Assistant Examiner: Stole, Einar
LREP Zelson, Esq., Steve T., Lambiris, Esq., Elias J.
CLMN Number of Claims: 62
ECL Exemplary Claim: 1
DRWN 10 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 5258
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to variants of cyclomaltodextrin glucanotransferase. More specifically the invention relates to a method of modifying the substrate binding and/or product selectivity of a precursor CGTase **enzyme**, and CGTase **variants** derived from a precursor CGTase enzyme by substitution, insertion and/or deletion of one or more amino acid residue(s), which amino acid residue(s) holds a position close to the substrate. Moreover, the invention relates to DNA constructs encoding the CGTase variants, expression vectors, host cells and methods of producing the CGTase variants of the invention.

L6 ANSWER 484 OF 926 USPATFULL
AN 1999:155509 USPATFULL
TI Kallikrein-inhibiting "Kunitz Domain" proteins and analogues thereof
IN Markland, Willaim, Milford, MA, United States
Ladner, Robert Charles, Ijamsville, MD, United States
PA Dyax Corp., Cambridge, MA, United States (U.S. corporation)
PI US 5994125 19991130
AI US 1998-136012 19980817 (9)
RLI Division of Ser. No. US 1996-676125, filed on 25 Sep 1996, now patented, Pat. No. US 5795685 which is a continuation-in-part of Ser. No. US 1994-208264, filed on 10 Mar 1994 which is a continuation-in-part of Ser. No. US 1994-179964, filed on 11 Jan 1994, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Degen, Nancy
LREP Yankwich, Leon R., Zwicker, Kenneth P.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2594
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Proteins are disclosed that are homologous to bovine pancreatic trypsin inhibitor (BPTI) Kunitz domains, and especially proteins that are homologous to lipoprotein-associated coagulation inhibitor (LACI) Kunitz domains, which inhibit one or more plasma and/or tissue kallikreins, and uses of such proteins in therapeutic and diagnostic methods also are disclosed. In particular, Kunitz domains derived from Kunitz domains of human origin and especially to the first Kunitz domain of LACI are disclosed.

L6 ANSWER 497 OF 926 USPATFULL
AN 1999:137004 USPATFULL
TI Method of preparing a **variant** of a lipolytic **enzyme**
IN Svendsen, Allan, Birker.o slashed.d, Denmark
Clausen, Ib Groth, Hiller.o slashed.d, Denmark
Okkels, Jens Sigurd, Frederiksberg C, Denmark
Thellersen, Marianne, Frederiksberg C, Denmark
PA Novo Nordisk A/S, Bagsv.ae butted.rt, Denmark (non-U.S. corporation)
PI US 5976855 19991102
AI US 1996-701339 19960822 (8)
RLI Continuation of Ser. No. WO 1995-DK79, filed on 22 Feb 1995
PRAI DK 1994-217 19940222
DT Utility
FS Granted

EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Saidha, Tekchand
LREP Zelson, Esq., Steve T., Lambiris, Esq., Elias J.
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 2008
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a method of preparing a **variant** of a parent lipolytic **enzyme**, comprising (a) subjecting a DNA sequence encoding the parent lipolytic enzyme to random mutagenesis, (b) expressing the mutated DNA sequence obtained in step (a) in a host cell, and (c) screening for host cells expressing a **mutated** lipolytic **enzyme** which has a decreased dependance to calcium and/or an improved tolerance towards a detergent or a detergent component as compared to the parent lipolytic enzyme.

L6 ANSWER 502 OF 926 USPATFULL
AN 1999:128499 USPATFULL
TI Peroxidase variants
IN Cherry, Joel R., Davis, CA, United States
Svendsen, Allan, Birker.o slashed.d, Denmark
Damhus, Ture, Copenhagen .O slashed., Denmark
Schneider, Palle, Ballerup, Denmark
PA Novo Nordisk A/S, Bagsvaerd, Denmark (non-U.S. corporation)
PI US 5968883 19991019
AI US 1999-235736 19990122 (9)
RLI Continuation of Ser. No. WO 1997-DK361, filed on 2 Sep 1997
PRAI DK 1996-937 19960903
DT Utility
FS Granted
EXNAM Primary Examiner: Gupta, Yogendra; Assistant Examiner: Garrett, Dawn L.
LREP Zelson, Esq., Steve T., Lambiris, Esq., Elias
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1561
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel variants of Coprinus cinereus peroxidase showing excellent hydrogen peroxide stability.

L6 ANSWER 524 OF 926 USPATFULL
AN 1999:81746 USPATFULL
TI Myceliophthora and scytalidium laccase variants
IN Pedersen, Anders Hjelholt, Lyngby, Denmark
Svendsen, Allan, Birker.o slashed.d, Denmark
Schneider, Palle, Ballerup, Denmark
Rasmussen, Grethe, Farum, Denmark
Cherry, Joel, Hellerup, Denmark
PA Novo Nordisk A/S, Bagsvaerd, Denmark (non-U.S. corporation)
PI US 5925554 19990720
AI US 1997-991531 19971216 (8)
PRAI DK 1996-1450 19961219
DK 1997-1020 19970908
US 1997-35414P 19970123 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Jacobson, Dian C.
LREP Zelson, Esq., Steve T., Green, Esq., Reza
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 725

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to laccase mutants with improved stability properties, in particular to Myceliophthora and Scytalidium laccase variants.

L6 ANSWER 536 OF 926 USPATFULL
AN 1999:43753 USPATFULL
TI Lipase variants
IN Svendsen, Allan, Birker.o slashed.d, Denmark
Patkar, Shamkant Anant, Lyngby, Denmark
Gormsen, Erik, Virum, Denmark
Clausen, Ib Groth, Hiller.o slashed.d, Denmark
Okkels, Jens Sigurd, Frederiksberg, Denmark
Thellersen, Marianne, Frederiksberg, Denmark
PA Novo Nordisk A/S, Bassvaerd, Denmark (non-U.S. corporation)
PI US 5892013 19990406
AI US 1995-488271 19950905 (8)
RLI Continuation-in-part of Ser. No. US 1995-434904, filed on 1 May 1995, now abandoned which is a continuation of Ser. No. US 1993-977429, filed on 22 Feb 1993, now abandoned
PRAI DK 1990-2194 19900913
DK 1990-2195 19900913
DK 1990-2196 19900913
DK 1993-466 19930423
DK 1994-217 19940222
DT Utility
FS Granted
EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Saidha, Tekchand
LREP Zelson, Steve T., Lamburis, Elais J.
CLMN Number of Claims: 39
ECL Exemplary Claim: 1
DRWN 10 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 2960
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to lipase variants which exhibit improved properties, detergent compositions comprising said lipase variants, DNA constructs coding for said lipase variants, and methods of making said lipase variants.

L6 ANSWER 585 OF 926 USPATFULL
AN 1998:143921 USPATFULL
TI Protease variants and compositions
IN Sierkstra, Laurens Nicolaas, Delft, Netherlands
Klugkist, Jan, Vlaardingen, Netherlands
Markvardsen, Peter, Bagsv.ae butted.rd, Denmark
von der Osten, Claus, Lyngby, Denmark
Bauditz, Peter, Koebenhavn, Denmark
PA Novo Nordisk A/S, Bagsv.ae butted.rd, Denmark (non-U.S. corporation)
PI US 5837517 19981117
AI US 1996-642987 19960506 (8)
PRAI DK 1995-519 19950505
EP 1995-201161 19950505
DK 1996-421 19960412
DT Utility
FS Granted
EXNAM Primary Examiner: Prouty, Rebecca E.; Assistant Examiner: Moore, William W.
LREP Zelson, Steve T., Lambiris, Elias J.
CLMN Number of Claims: 36
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 2189

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to enzymes produced by mutating the genes for a number of subtilases and expressing the mutated genes in suitable hosts are presented. The enzymes exhibit improved stability and/or improved wash performance in any detergent in comparison to their wild type parent enzymes. The enzymes are well-suited for use in any detergent and for some in especially liquid or solid shaped detergent compositions.

L6 ANSWER 589 OF 926 USPATFULL
AN 1998:138693 USPATFULL
TI Method for identifying active domains and amino acid residues in polypeptides and hormone variants
IN Wells, James A., Burlingame, CA, United States
Cunningham, Brian C., Piedmont, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
PI US 5834250 19981110
AI US 1997-903398 19970630 (8)
RLI Continuation of Ser. No. US 1995-483039, filed on 6 Jun 1995, now patented, Pat. No. US 5766854 which is a continuation of Ser. No. US 1994-190723, filed on 2 Feb 1994, now patented, Pat. No. US 5580723 which is a continuation of Ser. No. US 1992-960227, filed on 13 Oct 1992, now abandoned which is a continuation of Ser. No. US 1992-875204, filed on 27 Apr 1992, now abandoned which is a continuation of Ser. No. US 1989-428066, filed on 26 Oct 1989, now abandoned which is a continuation-in-part of Ser. No. US 1988-264611, filed on 28 Oct 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Achutamurthy, Ponnathapura
LREP Schwartz, Timothy R., Marschang, Diane L.
CLMN Number of Claims: 31
ECL Exemplary Claim: 1
DRWN 59 Drawing Figure(s); 52 Drawing Page(s)
LN.CNT 3240
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides methods for the systematic analysis of the structure and function of polypeptides by identifying active domains which influence the activity of the polypeptide with a **target** substance. Such active **domains** are determined by substituting selected amino acid segments of the polypeptide with an analogous polypeptide segment from an analog to the polypeptide. The analog has a different activity with the target substance as compared to the parent polypeptide. The activities of the segment-substituted polypeptides are compared to the same activity for the parent polypeptide for the target. A comparison of such activities provides an indication of the location of the active domain in the parent polypeptide. The invention also provides methods for identifying the active amino acid residues within the active domain of the parent polypeptide. The method comprises substituting a scanning amino acid for one of the amino acid residues within the active domain of the parent polypeptide and assaying the residue-substituted polypeptide so formed with a target substance. The invention further provides polypeptide variants comprising segment-substituted and residue-substituted growth hormones, prolactins and placental lactogens.

L6 ANSWER 592 OF 926 USPATFULL
AN 1998:134986 USPATFULL
TI Amylase variants
IN Bisg.ang.rd-Frantzen, Henrik, Lyngby, Denmark
Borchert, Torben Vedel, K.o slashed.benhavn, Denmark

Svendsen, Allan, Birker.o slashed.d, Denmark
Thellersen, Marianne, Frederiksberg, Denmark
Van der Zee, Pia, Virum, Denmark
PA Novo Nordisk A/S, Bagsvaerd, Denmark (non-U.S. corporation)
PI US 5830837 19981103
AI US 1994-343804 19941122 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Saidha, Tekchand
LREP Zelson, Esq., Steve T., Agris, Esq., Cheryl H.
CLMN Number of Claims: 42
ECL Exemplary Claim: 1
DRWN 12 Drawing Figure(s); 12 Drawing Page(s)
LN.CNT 2719
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A variant of a parent .alpha.-amylase enzyme having an improved washing and/or dishwashing performance as compared to the parent enzyme, wherein one or more amino acid residues of the parent enzyme have been replaced by a different amino acid residue and/or wherein one or more amino acid residues of the parent .alpha.-amylase have been deleted and/or wherein one or more amino acid residues have been added to the parent .alpha.-amylase **enzyme**, provided that the **variant** is different from one in which the methionine residue in position 197 of a parent B. licheniformis .alpha.-amylase has been replaced by alanine or threonine, as the only modification being made. The variant may be used for washing and dishwashing.

L6 ANSWER 603 OF 926 USPATFULL
AN 1998:104616 USPATFULL
TI Amylase variants
IN Bisg.ang.rd-Frantzen, Henrik, Lyngby, Denmark
Borchert, Torben Vedel, K.o slashed.benhavn, Denmark
Svendsen, Allan, Birker.o slashed.d, Denmark
Thellersen, Marianne, Frederiksberg, Denmark
Van der Zee, Pia, Virum, Denmark
PA Novo Nordisk A/S, Bagsvaerd, Denmark (non-U.S. corporation)
PI US 5801043 19980901
AI US 1995-459610 19950602 (8)
RLI Continuation of Ser. No. US 1994-343804, filed on 22 Nov 1994
PRAI DK 1993-1133 19931008
DK 1994-140 19940202
DT Utility
FS Granted
EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Saidha, Tekchand
LREP Zelson, Esq., Steve T., Agris, Esq., Cheryl H.
CLMN Number of Claims: 36
ECL Exemplary Claim: 1
DRWN 12 Drawing Figure(s); 12 Drawing Page(s)
LN.CNT 2728
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A variant of a parent .alpha.-amylase enzyme having an improved washing and/or dishwashing performance as compared to the parent enzyme, wherein one or more amino acid residues of the parent enzyme have been replaced by a different amino acid residue and/or wherein one or more amino acid residues of the parent .alpha.-amylase have been deleted and/or wherein one or more amino acid residues have been added to the parent .alpha.-amylase **enzyme**, provided that the **variant** is different from one in which the methionine residue in position 197 of a parent B. licheniformis .alpha.-amylase has been replaced by alanine or threonine, as the only modification being made. The variant may be used for washing and dishwashing.

L6 ANSWER 625 OF 926 USPATFULL
AN 1998:68781 USPATFULL
TI Method for identifying active domains and amino acid residues in polypeptides and hormone variants
IN Wells, James A., Burlingame, CA, United States
Cunningham, Brian C., Piedmont, CA, United States
PA Genentech, Inc., San Francisco, CA, United States (U.S. corporation)
PI US 5766854 19980616
AI US 1995-483039 19950606 (8)
RLI Continuation of Ser. No. US 1994-190723, filed on 2 Feb 1994, now patented, Pat. No. US 5580723 which is a continuation of Ser. No. US 1992-960227, filed on 13 Oct 1992, now abandoned which is a continuation of Ser. No. US 1992-875204, filed on 27 Apr 1992, now abandoned which is a continuation of Ser. No. US 1989-428066, filed on 26 Oct 1989, now abandoned which is a continuation-in-part of Ser. No. US 1988-264611, filed on 28 Oct 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Achutamurthy, Ponnathapura
LREP Skjerven, Morrill, MacPherson, Franklin & Friel, LLP, Terlizzi, Laura, Haliday, Emily M.
CLMN Number of Claims: 49
ECL Exemplary Claim: 1
DRWN 71 Drawing Figure(s); 54 Drawing Page(s)
LN.CNT 3362
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides methods for the systematic analysis of the structure and function of polypeptides by identifying active domains which influence the activity of the polypeptide with a **target** substance. Such active **domains** are determined by substituting selected amino acid segments of the polypeptide with an analogous polypeptide segment from an analog to the polypeptide. The analog has a different activity with the target substance as compared to the parent polypeptide. The activities of the segment-substituted polypeptides are compared to the same activity for the parent polypeptide for the target. A comparison of such activities provides an indication of the location of the active domain in the parent polypeptide. The invention also provides methods for identifying the active amino acid residues within the active domain of the parent polypeptide. The method comprises substituting a scanning amino acid for one of the amino acid residues within the active domain of the parent polypeptide and assaying the residue-substituted polypeptide so formed with a target substance. The invention further provides polypeptide variants comprising segment-substituted and residue-substituted growth hormones, prolactins and placental lactogens.

L6 ANSWER 626 OF 926 USPATFULL
AN 1998:65045 USPATFULL
TI Serine protease variants having peptide ligase activity
IN Abrahmsen, Lars, Stockholm, Sweden
Burnier, John, Pacifica, CA, United States
Wells, James A., Burlingame, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
PI US 5763256 19980609
AI US 1994-257467 19940608 (8)
RLI Continuation of Ser. No. US 1992-982010, filed on 24 Nov 1992, now abandoned which is a continuation of Ser. No. US 1990-566026, filed on 9 Aug 1990, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Hendricks, Keith D.

LREP Trecartin, Richard F.Flehr, Hohbach, Test, Albritton & Herbert
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN 22 Drawing Figure(s); 13 Drawing Page(s)
LN.CNT 1334
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to serine protease variants derived from precursor serine proteases via recombinant and/or chemical methods to form protease variants having improved peptide ligase activity. The invention also includes novel ligation substrates which in combination with the serine protease variants and a second ligation substrate are capable of forming a ligation product. The invention also relates to methods for forming such ligation products and the products formed thereby.

L6 ANSWER 632 OF 926 USPATFULL
AN 1998:51456 USPATFULL
TI Enrichment method for variant proteins having altered binding properties, M13 phagemids, and growth hormone variants
IN Garrard, Lisa J., Burlingame, CA, United States
Henner, Dennis J., Pacifica, CA, United States
Bass, Steven, Redwood City, CA, United States
Greene, Ronald, Durham, NC, United States
Lowman, Henry B., Hercules, CA, United States
Wells, James A., Burlingame, CA, United States
Matthews, David J., San Francisco, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
PI US 5750373 19980512
AI US 1993-50058 19930430 (8)
WO 1991-US9133 19911203
19930430 PCT 371 date
19930430 PCT 102(e) date
DT Utility
FS Granted
EXNAM Primary Examiner: Jagannathan, Vasu S.; Assistant Examiner: Carlson, K. Cochrane
LREP Winter, Daryl B., Dreger, Walter H.
CLMN Number of Claims: 50
ECL Exemplary Claim: 1
DRWN 22 Drawing Figure(s); 20 Drawing Page(s)
LN.CNT 3684
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for selecting novel proteins such as growth hormone and antibody fragment variants having altered binding properties for their respective receptor molecules is provided. The method comprises fusing a gene encoding a protein of interest to the carboxy terminal domain of the gene III coat protein of the filamentous phage M13. The gene fusion is mutated to form a library of structurally related fusion proteins that are expressed in low quantity on the surface of a phagemid particle. Biological selection and screening are employed to identify novel ligands useful as drug candidates. Disclosed are preferred phagemid expression vectors and selected human growth hormone variants.

L6 ANSWER 647 OF 926 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. DUPLICATE 44
AN 1998:164229 BIOSIS
DN PREV199800164229
TI Engineering of variants of the restriction endonuclease EcoRV that depend in their cleavage activity on the flexibility of sequences flanking the **recognition site**.
AU Wenz, Christian; Hahn, Meinhard; Pingoud, Alfred (1)
CS (1) Inst. Biochem., FB Biol., Justus-Liebig-Univ. Giessen,

Heinrich-Buff-Ring 58, D-35392 Giessen Germany
SO Biochemistry, (Feb. 24, 1998) Vol. 37, No. 8, pp. 2234-2242.
ISSN: 0006-2960.
DT Article
LA English
AB The present work describes **mutants** of the restriction **enzyme** EcoRV that discriminate very efficiently between oligodeoxynucleotide substrates with an EcoRV recognition sequence in different sequence context. All of these EcoRV variants harbor substitutions at position 226, where in the cocrystal structure of the specific EcoRV/DNA complex an arginine contacts the backbone of the DNA substrate upstream of the recognition sequence, and cleave an oligodeoxynucleotide with an EcoRV site in a nonflexible sequence context (the **recognition site** being flanked by runs of A and T) with much higher catalytic efficiency (kcat/Km) than an oligodeoxynucleotide with an EcoRV site in a flexible sequence context (the **recognition site** being flanked by runs of AT), in contrast to the wild-type enzyme, that cleaves both substrates with the same catalytic efficiency. Steady-state and single-turnover kinetics indicate that the enhanced selectivity of the mutants is due to the catalytic step of the reaction. It is possible to enhance the discriminatory power of these EcoRV variants through the choice of appropriate reaction conditions, in particular low salt concentration and low reaction temperatures. It must be emphasized that the enhanced selectivity of these EcoRV **variants** toward EcoRV **sites** in a flexible and nonflexible sequence context, respectively, is not only seen with oligodeoxynucleotides, but also with plasmid substrates.

L6 ANSWER 649 OF 926 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
DUPLICATE 45
AN 1999:1485 BIOSIS
DN PREV199900001485
TI Protein engineering of the restriction endonuclease EcoRV structure-guided design of **enzyme variants** that recognize the base pairs flanking the **recognition site**.
AU Schoettler, Sylvia; Wenz, Christian; Lanio, Thomas; Jeltsch, Albert; Pingoud, Alfred (1)
CS (1) Inst. Biochemie, Justus Liebig-Univ. Giessen, Heinrich-Buff-Ring 58, D-35392 Giessen Germany
SO European Journal of Biochemistry, (Nov., 1998) Vol. 258, No. 1, pp. 184-191.
ISSN: 0014-2956.
DT Article
LA English
AB We generated variants of the restriction endonuclease EcoRV that discriminate between **recognition sites** with different flanking sequences. This was achieved by designing new contacts to the bases in the major groove of the DNA preceding and following the EcoRV **recognition site**. We selected Ala181 as the starting point for the extension of the site specificity of EcoRV because, according to the structure of the specific EcoRV - DNA complex, this residue is involved in a water mediated contact with the bases flanking the recognition sequence on the 5' side. A substitution of this alanine residue by other amino acid residues changes the protein-DNA interface in this region and potentially creates new contacts, such that EcoRV variants could have an extended specificity, i.e. a greater selectivity for EcoRV sites within a particular sequence context. EcoRV variants with naturally occuring amino acid residues at position 181 were produced and their selectivity analyzed with oligodeoxynucleotide and plasmid substrates that differ only in the base pairs immediately flanking the EcoRV **site**. Some **variants**, having amino acid residues with long or bulky side chains at position 181 showed altered preferences for

the base pairs flanking the recognition sequence with oligodeoxynucleotide substrates without loosing their catalytic efficiency. One variant, A181K, is able to discriminate between purine and pyrimidine bases on the 5' side of the recognition sequence, probably by means of a new hydrogen bond to the N7 of the purine base. Another variant, A181E, strongly prefers a thymine base on the 5' side of the recognition sequence, presumably due to a hydrogen bond formed between the protonated glutamic acid residue and the O4 of thymine.

L6 ANSWER 691 OF 926 CAPLUS COPYRIGHT 2003 ACS
AN 1997:372344 CAPLUS
DN 127:105993
TI Variants of tissue-type plasminogen activator that display extraordinary resistance to inhibition by the serpin plasminogen activator inhibitor type 1
AU Tachias, Kathy; Madison, Edwin L.
CS Dep. Vascular Biology, Scripps Res. Inst., La Jolla, CA, 92037, USA
SO Journal of Biological Chemistry (1997), 272(23), 14580-14585
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Fibrinolysis is regulated in part by the interaction of tissue-type plasminogen activator (t-PA) and plasminogen activator inhibitor type 1 (PAI-1). Previous investigations suggest that three specific arginine residues, Arg-298, Arg-299, and Arg-304 of t-PA, play a crit. role in this important regulatory interaction. Our earlier studies have demonstrated that conversion of any of these three residues to a glutamic acid residue reduced the rate of inhibition of t-PA by PAI-1 by factors varying from 58-64. In addn., we have reported that the second order rate const. for inhibition by PAI-1 of the variant t-PA/K296E,R298E,R299E is reduced by a factor of approx. 2800 compared with that of wild type t-PA. In this study, we have significantly extended our earlier observations by identifying t-PA variants that are substantially more resistant to inhibition by PAI-1 than any previously reported variants of t-PA or urokinase-type plasminogen activator. Single-chain t-PA/R275E,R298E,R299E,R304E, for example, is inhibited by PAI-1 approx. 120,000 times less rapidly than single-chain, wild type t-PA. We also report the first direct comparison of the effects of charge reversal mutations of Agr-298, Arg-299, and/or Arg-304 on the properties of the single- and two-chain forms of t-PA. While these mutations confer extraordinary resistance to inhibition by PAI-1 to both forms of the enzyme, our observations reveal that the single-chain enzyme is affected to a greater extent than the two-chain enzyme. Two-chain, while type t-PA is inhibited by PAI-1 approx. 1.4 times more rapidly than single-chain t-PA. The corresponding ratio increases to 7.6 or 6.7, resp., for variants of t-PA contg. the R298E,R299E or R298E,R299E,R304E mutations.

L6 ANSWER 741 OF 926 CAPLUS COPYRIGHT 2003 ACS
AN 1996:593995 CAPLUS
DN 125:241710
TI Furilisin: a variant of subtilisin BPN' engineered for cleaving tribasic substrates
AU Ballinger, Marcus D.; Tom, Jeffrey; Wells, James A.
CS Department of Protein Engineering, Genentech Inc., South San Francisco, CA, 94080, USA
SO Biochemistry (1996), 35(42), 13579-13585
CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
AB Subtilisin BPN' was engineered to cleave proteins after tribasic sequences

in a manner that resembles the substrate specificity of furin, one of the mammalian subtilisin homologs that processes prohormones. As a starting point, the authors used a double mutant of subtilisin BPN' (N62D/G166D; kexilisin) that showed substantial preference for cleaving after sequences having consecutive dibasic residues (namely, at the P1 and P2 substrate positions). Addnl. specificity for basic residues was engineered at the P4 position by introducing subtilisin-to-furin substitutions at 3 hydrophobic residues that composed the S4 subsite (Tyr-104, Ile-107, and Leu-126). Initial attempts to incorporate a Y104D or I107E mutation or the Y104D/I107E double **mutation** into the dibasic-specific **enzyme** failed to generate the processed enzyme. The problem was traced to the inability of the mutant prosubtilisins to process themselves and fold correctly. Replacing the natural processing site sequence (AHAY) with a good furin substrate sequence (RHKR) resulted in expression of the triple subtilisin mutant (N62D/Y104D/G166D) designated furilisin. Furilisin hydrolyzed synthetic tribasic substrates (succinyl-RAKR-pNA or succinyl-KAKR-pNA) with high catalytic efficiency (kcat/Km = >3 .times. 105 M-1 s-1) and discriminated in favor of Arg vs. Ala at the P4 position by a factor of 360. The overall specificity change vs. the wild-type enzyme was dramatic. For example, succinyl-RAKR-pNA was cleaved .apprx.60,000-fold faster than succinyl-AAPF-pNA, a good substrate for wild-type subtilisin. Similarly, furilisin was inhibited (Ki* = 29 nM) by a variant of the turkey ovomucoid 3rd domain inhibitor that contained an engineered furin substrate site (RCKR.dwnarw.) and not by one having a good wild-type subtilisin substrate sequence (ACTL.dwnarw.). Interestingly, the extreme changes in substrate specificity resulted from substantial synergy between the engineered subsites. These studies provide a basic example of how to manipulate substrate specificity in a modular fashion, thereby creating an engineered enzyme that may be useful as a protein processing tool.

L6 ANSWER 743 OF 926 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 51
AN 1996:586591 CAPLUS
DN 125:241648
TI Kinetic and thermodynamic studies of NADP+ binding to human erythrocyte glucose-6-phosphate dehydrogenase **variants**: The **binding site** and the enthalpy-entropy compensation phenomenon
AU Adediran, S. A.
CS Department Chemistry, University Ilorin, Ilorin, Nigeria
SO Biokemistri (1996), 6(1), 31-37
CODEN: BIOKE3
PB Klobex Academic Publishers
DT Journal
LA English
AB The binding of NADP to human erythrocyte glucose 6-phosphate dehydrogenase variants was studied as a function of pH and temp. in Tris-borate and Tris-triethylamine buffers of const. ionic strength of 0.001M. From the linearity and the slopes of T.DELTA.S vs. .DELTA.H plots, the **binding sites** are proven not to be part of the structural locus and the interchain link of each of the **enzyme variants**. The compensation temp., Tc of about 310 K obtained in this study for all the **enzyme variants** with the harmonic mean of exptl. temp. of 303.3 K, confirms that the compensation patterns in aq. medium are an intrinsic property of all protein reactions. The enthalpy-entropy compensation obsd. for glucose 6-phosphate dehydrogenase reactions may be intimately lined to the same configurational change that has an important control on the reactivity of the enzyme in vivo.

L6 ANSWER 748 OF 926 USPATFULL
AN 95:90514 USPATFULL
TI Protease nexin-I variants

IN Scott, Randy W., Sunnyvale, CA, United States
Golini, Fred, San Mateo, CA, United States
McGrogan, Michael, San Carlos, CA, United States
PA Incyte Pharamaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 5457090 19951010
AI US 1992-924294 19920803 (7)
RLI Continuation of Ser. No. US 1990-542484, filed on 21 Jun 1990, now patented, Pat. No. US 5187089
DT Utility
FS Granted
EXNAM Primary Examiner: Schwartz, Richard A.; Assistant Examiner: Schmickel, D.
LREP Francis, Carol L., Bozicevic, KarlFish & Richardson
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 1221
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB One or more amino acid residues within the reactive site region of protease nexin-I are altered in order to create analogs or variants of protease nexin-I. These analogs have substantially different protease specificities as well as different effects on regulating the activity of proteolytic enzymes which enzymes have substantial effects on a number of different physiological functions. Formulations containing the protease nexin-I variants and methods for administering these formulations to obtain desirable therapeutic results are disclosed.

L6 ANSWER 764 OF 926 MEDLINE DUPLICATE 54
AN 96046661 MEDLINE
DN 96046661 PubMed ID: 7577984
TI pH, electrolyte, and substrate-linked variation in active **site** structure of the Trp51Ala **variant** of cytochrome c peroxidase.
AU Turano P; Ferrer J C; Cheesman M R; Thomson A J; Banci L; Bertini I; Mauk A G
CS Department of Chemistry, University of Florence, Italy.
SO BIOCHEMISTRY, (1995 Oct 24) 34 (42) 13895-905.
Journal code: 0370623. ISSN: 0006-2960.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199512
ED Entered STN: 19960124
Last Updated on STN: 19990129
Entered Medline: 19951214
AB Electronic absorption, MCD, and 1H NMR spectroscopy have been used to characterize the structures and linkage relationships of three active site states, LS1, HS, and LS2, of the Trp51Ala variant of yeast cytochrome c peroxidase (CcP) in the Fe(III) state. In addition, the binding of three substrates (styrene, catechol, and guaiacol) to the Fe(III) variant has been studied by 1H NMR spectroscopy, and the paramagnetically shifted resonances of the cyanide adduct of the variant have been assigned. The heme iron is hexacoordinated in all three pH-dependent states of the enzyme. LS1, the dominant acidic species, exhibits electronic and MCD spectra indicative of low-spin, bis-histidine coordination environment for the heme iron. The HS form, which dominates at intermediate pH, exhibits electronic, MCD, and 1H NMR spectra characteristic of high-spin heme Fe(III) with axial histidyl and water ligands. The LS2 species exhibits spectroscopic properties indicative of a bis-histidine, low-spin Fe(III) derivative. The equilibrium constants for interconversion of these forms of the **variant enzyme** are highly dependent on ionic

strength, specific anions, and temperature of the solution, with the HS form stabilized relative to the other forms in the presence of several noncoordinating, anionic species. Aromatic substrates such as styrene, catechol, and guaiacol affect the chemical shifts of the heme substituents of the HS species but not of the LS2 species. Based on these results, a model is proposed that accounts to a large extent for the electrostatic origin of the three forms of the active **site** of the Trp51Ala **variant** and the mechanisms by which they are differentially stabilized in solution.

L6 ANSWER 769 OF 926 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V. DUPLICATE
AN 1995:25170940 BIOTECHNO
TI Successive organophosphate inhibition and oxime reactivation reveals distinct responses of recombinant human cholinesterase variants
AU Schwarz M.; Loewenstein-Lichtenstein Y.; Glick D.; Liao J.; Norgaard-Pedersen B.; Soreq H.
CS Department of Biological Chemistry, The Life Sciences Institute, The Hebrew University of Jerusalem, 91904 Jerusalem, Israel.
SO Molecular Brain Research, (1995), 31/1-2 (101-110)
CODEN: MBREE4 ISSN: 0169-328X
DT Journal; Article
CY Netherlands
LA English
SL English
AB To explore the molecular basis of the biochemical differences among acetylcholinesterase (AChE), butyrylcholinesterase (BuChE) and their alternative splicing and allelic variants, we investigated the acylation phase of cholinesterase catalysis, using phosphorylation as an analogous reaction. Rate constants for organophosphate (DFP) inactivation, as well as for oxime (PAM)-promoted reactivation, were calculated for antibody-immobilized human cholinesterases produced in Xenopus oocytes from natural and **site**-directed **variants** of the corresponding DNA constructs. BuChE displayed inactivation and reactivation rates 200- and 25-fold higher than either product of 3'-variable AChE DNAs, consistent with a putative in vivo function for BuChE as a detoxifier that protects AChE from inactivation. Chimeric substitution of active site gorge-lining residues in BuChE with the more anionic and aromatic residues of AChE, reduced inactivation 60-fold but reactivation only 4-fold, and the rate-limiting step of its catalysis appeared to be deacylation. In contrast, a positive charge at the acyl-**binding site** of BuChE decreased inactivation 8-fold and reactivation 30-fold. Finally, substitution of Asp70 by glycine, as in the natural 'atypical' BuChE variant, did not change the inactivation rate yet reduced reactivation 4-fold. Thus, a combination of electrostatic active site charges with aromatic residue differences at the gorge lining can explain the biochemical distinction between AChE and BuChE. Also, gorge-lining residues, including Asp70, appear to affect the deacylation step of catalysis by BuChE. Individuals carrying the 'atypical' BuChE allele may hence be unresponsive to oxime reactivation therapy following organophosphate poisoning.

L6 ANSWER 800 OF 926 USPATFULL
AN 93:74072 USPATFULL
TI Method of treating thromboembolic disorders by administration of diglycosylated t-PA variants
IN Burck, Philip J., Indianapolis, IN, United States
Jackson, Charles V., Indianapolis, IN, United States
Smith, Gerald F., Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5242688 19930907

AI US 1990-633584 19901224 (7)
DT Utility
FS Granted
EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Walsh, Stephen
LREP Plant, Thomas G., Whitaker, Leroy
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 17 Drawing Figure(s); 17 Drawing Page(s)
LN.CNT 1920
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a method of treating thromboembolic disorders with the diglycosylated form of a tissue plasminogen activator derivative that lacks the Finger, EGF and Kringle I domains of the native tissue plasminogen activator molecule.

L6 ANSWER 807 OF 926 USPATFULL
AN 93:12449 USPATFULL
TI Protease nexin-I variants which inhibit elastase
IN Scott, Randy W., Sunnyvale, CA, United States
Golini, Fred, San Mateo, CA, United States
McGrogan, Michael, San Carlos, CA, United States
PA Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 5187089 19930216
AI US 1990-542484 19900621 (7)
DT Utility
FS Granted
EXNAM Primary Examiner: Wehmar, Elizabeth C.; Assistant Examiner: Crouch, Deborah
LREP Morrison & Foerster
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 1089
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB One or more amino acid residues within the reactive site region of protease nexin-I are altered in order to create analogs or variants or protease nexin-I. These analogs have substantially different protease specificities as well as different effects on regulating the activity of proteolytic enzymes which enzymes have substantial effects on a number of different physiological functions. Formulations containing the protease nexin-I variants and methods for administering these formulations to obtain desirable therapeutic results are disclosed.

Requested

L6 ANSWER 808 OF 926 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
DUPLICATE 63
AN 1993:432283 BIOSIS
DN PREV199396086908
TI Conserved sequence motif DPPY in region IV of the phage T4 Dam DNA-(N-6-adenine)-methyltransferase is important for S-adenosyl-L-methionine binding.
AU Kossykh, Valeri G.; Schlagman, Samuel L.; Hattman, Stanley
CS Dep. Biol., Univ. Rochester, Rochester, NY 14627 USA
SO Nucleic Acids Research, (1993) Vol. 21, No. 15, pp. 3563-3566.
ISSN: 0305-1048.
DT Article
LA English
AB Comparison of the deduced amino acid sequences of DNA-(N-6-adenine)-methyltransferases has revealed several conserved regions. All of these enzymes contain a DPPY-**motif**, or a **variant** of it. By **site**-directed mutagenesis of a cloned T4 dam gene, we have altered the first proline residue in this motif (located in conserved region IV of

the T4 Dam-MTase) to alanine or threonine. The mutant enzymic forms, P172A and P172T, were overproduced and purified. Kinetic studies showed that compared to the wild-type (wt) the two mutant enzymic forms had: (i) an increased (6 and 23-fold, respectively) K-m for substrate, S-adenosylmethionine (AdoMet) and an increased (6 and 23-fold) K-i for product, S-adenosyl-homocysteine (AdoHcy); (ii) a slightly reduced (1.5 and 3-fold lower) k-cat; (iii) a strongly reduced k-cat/K-m-AdoMet (10 and 80-fold); and (iv) the same K-m for substrate DNA. Equilibrium dialysis studies showed that the **mutant enzymes** had a reduced (3 and 7-fold lower) K-a for AdoMet; all forms bound two molecules of AdoMet. Taken together these data indicate that the P172A and P172T alterations resulted primarily in a reduced affinity for AdoMet. This suggests that the DPPY-**motif** is important for AdoMet-**binding**, and that region IV contains an AdoMet-**binding site**.

Requested

L6 ANSWER 822 OF 926 CAPLUS COPYRIGHT 2003 ACS
AN 1993:76032 CAPLUS
DN 118:76032
TI Functional analysis of box I mutations in yeast site-specific recombinases Flp and R: Pairwise complementation with recombinase **variants** lacking the active-**site** tyrosine
AU Chen, Jing Wen; Evans, Barbara R.; Yang, Sang Hwa; Araki, Hiroyuki; Oshima, Yasuji; Jayaram, Makkuni
CS Dep. Microbiol., Univ. Texas Austin, Austin, TX, 78712, USA
SO Molecular and Cellular Biology (1992), 12(9), 3757-65
CODEN: MCEBD4; ISSN: 0270-7306
DT Journal
LA English
AB The site-specific recombinases Flp and R from Saccharomyces cerevisiae and Zygosaccharomyces rouxii, resp., are related proteins that belong to the yeast family of site-specific recombinases. They share approx. 30% amino acid matches and exhibit a common reaction mechanism that appears to be conserved within the larger integrase family of site-specific recombinases. Two regions of the proteins, designated box I and box II, also harbor a significantly high degree of homol. at the nucleotide sequence level. The properties of Flp and R variants carrying point mutations within the box I segment were examd. for substrate-**binding**, DNA cleavage, and full-**site** and half-site strand transfer reactions. All mutations abolish or seriously diminish recombinase function either at the substrate-binding step or at the catalytic steps of strand cleavage or strand transfer. Of particular interest are mutations of Arg-191 of Flp and R, residues which correspond to one of the two invariant arginine residues of the integrase family. These variant proteins bind substrate with affinities comparable to those of the corresponding wild-type recombinases. Among the binding-component variants, only Flp(R191K) is capable of efficient substrate cleavage in a full recombination target. However, this protein does not cleave a half recombination site and fails to complete strand exchange in a full site. Strikingly, the Arg-191 mutants of Flp and R can be rescued in half-site strand transfer reactions by a second point mutant of the corresponding recombinase that lacks its active-site tyrosine (Tyr-343). Similarly, Flp and R variants at Cys-189 and Flp variants at Asp-194 and Asp-199 can also be complemented by the corresponding Tyr-343-to-phenylalanine recombinase mutant.

L6 ANSWER 864 OF 926 DGENE (C) 2003 THOMSON DERWENT
AN AAB29107 Protein DGENE
TI Identifying variant recombinases mediating recombination at **variant sites** (vRS) by contacting a mutant recombinase, a first and second vRS having a reporter gene, and a second nucleic acid having 2 vRS and a reporter gene -

IN Sauer B L; Rufer A W
PA (OKLA-N) OKLAHOMA MEDICAL RES FOUND.
PI WO 2000060091 A2 20001012 144p
AI WO 2000-US9154 20000406
PRAI US 1999-127977 19990406
DT Patent
LA English
OS 2000-665010 [64]
AB The present invention relates to the identification of recombinase variants which have an altered specificity. They are tested using constructs containing **variant recognition sites**, which are not recognised by non-mutant recombinase but undergo recombination in the presence of a **variant enzyme**. **Variant** recombinases are useful in the production of genetically modified crop plants, particularly seedless varieties, and in phage packaging, which has uses in cloning.

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